interventions that lead to demonstrable changes in the natural history of untreated illness. There is no such evidence available in Alzheimer's disease. The randomized trials of tacrine (Cognex) and donepezil (Aricept) enrolled subjects who would generally be considered to have moderate, not early, dementia. For instance, the mean Mini Mental Status score of participants in the tacrine trials was 16 to 19 out of 30, a score indicating moderate impairment.[7] Although donepezil trials have included some patients with higher scores, most are in the 18 to 21 range[8]; there are no published long-term studies with patients having scores exclusively in the 21 to 26 range. These studies also have excluded all patients with comorbid conditions. Even if positron emission tomographic scanning can be shown to reliably detect those with Alzheimer's before the onset of clinical symptoms, treatment studies would be needed to demonstrate such early detection is beneficial.

To be judged beneficial, early treatment would need to show improvements in cognition, physical function, behavioral problems, or cost savings. Unfortunately, in many cases the "improvements" in cognition in trials of cholinesterase inhibitors were not detectable to families or clinicians.[9] It is doubtful that early diagnosis with positron emission tomographic scanning would allow treatment to improve physical function (eg, Activities of Daily Living) because these functions are not affected in the early phases of the disease. A decline in functional ability, not cognition, is what stresses families most and leads to placement in nursing homes. No randomized, placebo-controlled trials of cholinesterase inhibitors have shown a reduction in nursing home placement. Vitamin E has been shown in one randomized trial to reduce nursing home utilization and maintain function, but this study also involved subjects with more advanced dementia so it does not answer the question whether early treatment will reduce long-term costs.[10]

Finally, there is an ethical dilemma to early diagnosis of dementia. Diagnosis "2 to 3 years before manifestation of dementia-related symptoms" would only be acceptable if treatment at that stage led to marked improvements in outcomes. Without such hope for treatment early diagnosis would be cruel. Consider the psychological impact on the patient, a person's employment or insurance coverage, or the effect on the family if we were to diagnose dementia before we were able to make a meaningful difference in their lives through treatment.

Prospective, controlled trials in representative populations (ie, those in primary care settings who have typical comorbid conditions) are needed. Such trials must measure meaningful outcomes such as caregiver burden, costs, and functional changes that are appreciated by untrained family members. When evidence exists that early diagnosis and treatment is beneficial, then positron emission tomography and treatments such as cholinesterase inhibitors can be considered the standard of care and worthy of insurance coverage. In the meantime, we should redouble our efforts to educate family members in the recognition of cognitive changes, primary care physicians how best to diagnose and manage dementia, and advocate to managed care plans and other forms of insurance payers to adequately fund management of this devastating disease.

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Correction

We regret the omission of Ronald M Davis and Edward H Wagner as co-authors of the call for papers addressing chronic disease management in the June issue of wjm.